REMARKS

In the Office Action, claims 2, 8-13, 20-27, 32-34 and 43 are rejected under 35 U.S.C. §112, ¶2; claims 1 and 3-7 are rejected under 35 U.S.C. §102; and claims 1, 3-8, 14-18, 20, 22, 24, 28, 32-36, 38-39, 40-41 and 43-44 are rejected under 35 U.S.C. §103. Claims 1, 2, 8, 15, 20, 21, 24, 25, 38 and 43 have been amended; claims 45-49 have been withdrawn; and claims 50-55 have been newly added. Applicants believe that the rejections have been overcome or are improper in view of the amendments and for the reasons set forth below.

At the outset, the Patent Office indicates that claims 19, 29-31, 37 and 42 are free of cited prior art. See, Office Action Summary. In response, Applicants have added claims 50-55 to incorporate the limitations of claims 19, 29-31, 37 and 42, respectfully, including the limitations from the claims from which they depend. Further, claims 19, 29-31, 37 and 42 have been cancelled without prejudice or disclaimer in response to same. Therefore, newly added claims 50-55 should be allowed.

In the Office Action, claims 2, 8-13, 20-27, 32-34 and 43 are rejected under 35 U.S.C. §112, ¶2. More specifically, the Patent Office alleges that the claim term "by weight of the amino acids", such as defined in claim 2, is indefinite. Further, the Patent Office alleges that the claim term "a daily recommended amount of threonine," such as defined in claim 32, is indefinite.

With respect to the claim term "by weight of the amino acids", Applicants have amended claim 2 in addition claims 1, 8, 15, 20-21, 24, 25, 38 and 43 to now recite "by weight of the protein source". Support for this amendment can be found, for example, on page 11 at line 3 of the specification. See also, Specification, page 7, line 22 to page 8, line 2. Applicants note for the record that this amendment was made for clarification purposes and thus was not intended to narrow and/or disclaim any subject matter in view of same. Thus, Applicants believe that the rejection has been overcome with respect to same.

As previously discussed, the Patent Office also alleges that claims 32-34 are indefinite with respect to the claim term "a daily recommended amount of threonine." Applicants believe that the Patent Office's position is improper.

As defined in claims 32-34, the amount of threonine in the diet is based on a percentage of the recommended daily amount. Indeed, one skilled in the art should readily understand the recommended daily amount of threonine for a diet even if this may vary from patient-type to patient-type (i.e., adult verses child), based on known and used standards (e.g., government standards) regarding same. Thus, as the claims at issue define a percentage of the recommended daily amount of threonine, the scope and content of same should be readily understood to one skilled in the art. Therefore, Applicants believe that the claimed invention fully complies with 35 U.S.C. §112, ¶2.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

In the Office Action, claims 1 and 3-7 are rejected under 35 U.S.C. §102 as anticipated by U.S. Patent No. 6,468,987 ("*Demichele*"). The Patent Office essentially asserts that *Demichele* discloses each of the features of the claimed invention as defined by claims 1 and 3-7. Applicants believe that this rejection is improper.

Of claims 1 and 3-7, claim 1 is the sole independent claim. Claim 1 relates to a method of treating a disease state characterized by alterations to the mucin levels in a patient. The method includes enterally administering to the patient a nutritional composition that has a protein source including amino acids wherein threonine comprises at least 5.5% by weight of the protein source. Applicants have discovered that mucin production can be maintained, improved or increased by administering a therapeutically effective amount of threonine to a patient, thus facilitating treatment of a disease state that can impair or reduce mucin production in the patient.

In contrast, Applicants believe that the *Demichele* reference is deficient with respect to the claimed invention. For example, nowhere does this reference disclose or arguably suggest that a therapeutically effective amount of threonine can be administered to the patient in order to treat disease in the patient that can alter mucin levels. The primary focus of *Demichele* relates to the use of a composition that includes indigestible carbohydrates and poly-unsaturated fatty acids in the treatment of ulcerative colitis. This reference suggests that these two components can act together to promote the incorporation of small n-3 fatty acids into colonocytes at the expense of n–6 fatty acids thereby increasing the rate of the incorporation of the n-3 series into the colonic mucosal phosolipids, thus modulating the rate of local eicosanoid generation by the gastrointestinal mucosa. Indeed, threonine is not involved in this process at all. Therefore, while

local eicosanoid generation by the gastrointestinal mucosa may be modulated by diet and thus inflammation may be reduced as *Demichele* arguably suggests, this is a completely different mechanism of operation from the synthesis of mucins (e.g., the main component of the substance which protects the gastrointestinal mucosa), that is promoted by the administration of a therapeutically effective amount of threonine, let alone threonine in an amount of at least 5% by weight of the protein source as required by the claimed invention.

Further, Applicants believe that the Patent Office's position with respect to the amount of threonine disclosed in *Demichele* is incorrect. For example, table 12 shows that the threonine content is 4.34% of the amino acids. Clearly, this is below the amount of threonine as specified in claim 1.

Moreover, the Patent Office's calculation is based on theory that contradicts what *Demichele* discloses. Again, table 12 provides a threonine content of 4.34% as discussed above. Thus, the Patent Office's calculation is unnecessary as well as inaccurate where the difference between the theoretical value of 5.6% (as calculated by the Patent Office) and the actual value of 4.34% (as disclosed in *Demichele*) underlies that it is not the fact that whey was used but how the whey was produced that is important. Therefore, Applicants believe that one skilled in the art would consider what *Demichele* allegedly discloses and the claimed invention to be distinguishable.

Based on at least these reasons, Applicants believe that *Demichele* fails to disclose or arguably suggest the claimed invention. Therefore, Applicants respectfully submit that *Demichele* fails to anticipate the claimed invention.

Accordingly, Applicants respectfully request that the anticipation rejection is withdrawn.

In the Office Action, claims 1, 3-8, 14-18, 20, 22, 24, 28, 32-26, 38-39, 40-41 and 43-44 are rejected under 35 U.S.C. § 103 in view of *Hennebicq–Reig* taken with *Bertolo*, *Demichele*, *Pearson*, and U.S. Patent No. 6,187,558 ("*Granados*"). The Patent Office primarily relies on the *Hennebicq-Reig* reference and thus relies on the remaining cited art to remedy the deficiencies of same. Applicants believe that this rejection is improper.

Of the pending claims at issue, claims 1, 8, 14, 20, 24, 28, 32, 35 and 40 are the sole independent claims. Claim 1 relates to a method for treating a disease state characterized by alterations to the mucin levels to a patient. The method includes enterally administering to the

patient a nutritional composition which has a protein source including amino acids wherein threonine comprises at least 5.5% by weight of the protein source. Claim 8 relates to a method for maintaining the synthesis of mucins in a patient. The method includes enterally administering to the patient a nutritional composition which has a protein source including amino acids wherein threonine comprises at least 5.5% by weight of the protein source.

Claim 14 recites a method for maintaining a synthesis of mucins in a patient. The method includes enterally administering to the patient a nutritional composition which includes a protein source that contains a therapeutically effective amount of threonine, a carbohydrate source and a lipid source including a mixture of medium chain triglycerides and long chain triglycerides. Claim 20 recites a method of treating a disease state characterized by alterations to the mucin level in a patient. The method includes enterally administering to the patient a nutritional composition that has a protein source including amino acids wherein threonine comprises at least 7.4% by weight of the protein source. Claim 24 recites a method for maintaining the synthesis of mucins in a patient. The method includes enterally administering to the patient a nutritional composition that has a protein source including amino acids wherein threonine comprises at least 7.4% by weight of the protein source.

Claim 28 recites a method for increasing the synthesis of mucins in a patient. The method includes supplementing a diet of the patient by adding a therapeutically effective amount of threonine to the diet. Claim 32 recites a method for increasing the synthesis of mucins in a patient. The method includes administering to the patient a nutritional composition which has a protein source containing threonine at least 30% of a daily recommended amount of threonine. Claim 35 recites a method of treating intestinal inflammation in a patient. The method includes administering to the patient a therapeutically effective amount of threonine. Claim 40 recites a method for treating intestinal bacterial infection in a patient. The method includes administering a nutritional composition to the patient wherein the nutritional composition contains a therapeutically effective amount of threonine.

Applicants have conducted a number of experiments to demonstrate the beneficial effects of the claimed invention. For example, Applicants have demonstrated with both *in vitro* and *in vivo* studies that threonine supplementation can be an effective and efficient nutritional strategy to increase or restore the mucoprotein synthesis rate, and thus to insure a better epithelial cell

protection. See, Specification, Examples 3 and 4, pages 12-13. Further, Applicants have demonstrated that mucus conditions in patients can improve after administering the nutritional composition according to an embodiment of the present invention as described in Example 2. This resulted in the remission of Crohn's disease in most of the patients who were diagnosed as suffering from Crohn's disease. See, Specification, page 12, lines 5-8.

In contrast, Applicants believe that the cited art, even if combinable, fails to disclose or suggest the claimed invention. With respect to the primary reference, indeed, the Examiner even admits that this reference fails to disclose the use of threonine and/or threonine enriched nutritional compositions for maintaining or increasing mucin. See, Office Action, page 6-7.

Further, this reference fails to suggest the importance of threonine for mucin synthesis contrary to the Patent Office's position. Indeed, table 4 as disclosed in this reference merely shows that threonine is a significant component of mucins. Thus, the *Hennebicq-Rei*g reference, on its own, is clearly deficient with respect to the claimed invention.

Contrary to the Patent Office's position, the remaining cited art cannot be relied on, alone or even if combinable, to remedy the deficiencies of the *Hennebicq-Reig* reference. At the outset, Applicants question whether the remaining cited art should be combined with *Hennebicq-Reig* reference in the first place. For example, the primary focus of the *Hennebicq-Reig* reference relates to the response of malignant mucin secreting cells to treatment with a specific drug. In contrast, the *Bertolo* reference relates to a comparison of the responses of newly born piglets to parental and enteral feeding, thus attempting to determine the highest safe level of threonine intake by the two methods. Indeed, the technical aspects as disclosed in the *Hennebicq-Reig* and *Bertolo* references are very different and thus would not lead one skilled in the art to combine, let alone modify same, based on these differences.

With respect to the *Demichele* reference, indeed, threonine is not involved in the process disclosed therein that relates to the modulation of local eicocanoid generation by the cells of the gastrointestinal mucosa as discussed above. With respect to the *Granados* reference, this reference relates to mucins in insects. Moreover, the *Pearson* reference merely suggests that damage to the protective mucus layer appears to be associated with inflammation of the gastrointestinal mucosa in calves. This provides little, if any additional understanding, to what is known in the art. Indeed, Applicants have even acknowledged that ulcerative colitis is known to

be associated with alterations in mucin synthesis. See, Specification, page 2, lines 3-8. What the Patent Office clearly has done is to rely on hindsight reasoning in an attempt to combine and/or modify the cited art to arrive at the claimed invention. Clearly this is improper.

Even assuming that the cited art can be properly combined, the combined teachings of same are still deficient with respect to the claimed invention. Again, the primary *Hennebicq-Reig* reference is clearly deficient with respect to the claimed invention. With respect to *Bertolo*, this article merely suggests a connection between a decrease threonine requirement and gut atrophy. They argue that the decrease is linked to the bypass of the splancnic organs, particularly the gastrointestinal tract which induces specifically high threonine requirement because threonine is a critical amino acid for the synthesis of mucin at the surface of the small intestine. This is reinforced by the fact that TPN induces mucosal atrophy. In contrast, the claimed invention requires administering a therapeutically effective amount of threonine to a patient in order to increase, maintain or improve mucin production and thus further facilitate the treatment of a disease state that is capable of altering mucin levels in the patient.

Further, the *Demichele* reference is deficient as discussed above. For example, the primary focus of this reference relates to treating ulcerative colitis through the administration of a composition that includes ingestible carbohydrates and poly-unsaturated fatty acids. Again, threonine is not even involved in this process.

With respect to the *Granados* reference, the Patent Office merely relies on same for its purported teachings relating to the protective function of mucin in intestinal mucosal layer, that mucin plays an active role in preventing bacterial infection, and that mucin is rich in threonine. Yet, this does not suggest that the administration of an effective amount of threonine to a patient can maintain, improve or increase mucin production in the patient, thus leading to the treatment of disease that can alter mucin level in the patient as required by the claimed invention. Moreover, *Granados* relates to mucins in insects. With respect to *Pearson*, the Patent Office merely relies on same for its purported teachings regarding the association of ulcerative colitis with alteration of mucin synthesis.

Based on at least these noted reasons, Applicants believe that the cited art fails to disclose or suggest at least a number of features of the claim invention. Therefore, Applicants

respectfully submit that the cited art, even if combinable, fails to render obvious the claimed invention.

Accordingly, Applicants respectfully request that the obvious rejection be withdrawn.

For the foregoing reasons, Applicants respectfully submit that the application is in condition for allowance and earnestly solicit reconsideration the same.

Respectfully submitted,

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